



## ABCC8 gene

ATP binding cassette subfamily C member 8

### Normal Function

The *ABCC8* gene provides instructions for making the sulfonylurea receptor 1 (SUR1) protein. The SUR1 protein is one part (subunit) of the ATP-sensitive potassium (K-ATP) channel that is found across cell membranes in the beta cells of the pancreas. Beta cells secrete insulin, which is a hormone that helps control blood sugar levels. Insulin controls how much sugar (in the form of glucose) is passed from the bloodstream into cells to be used as energy. The K-ATP channel controls the secretion of insulin out of beta cells and into the bloodstream. These channels open and close in response to the amount of glucose in the bloodstream, which helps regulate insulin secretion and control blood sugar levels. The closing of the channels results in a process that triggers insulin secretion by beta cells.

### Health Conditions Related to Genetic Changes

#### congenital hyperinsulinism

More than 300 mutations in the *ABCC8* gene have been found to cause congenital hyperinsulinism. This condition causes frequent episodes of low blood sugar (hypoglycemia), decreased energy, and irritability. Most of these mutations change single protein building blocks (amino acids) in the SUR1 protein.

Some *ABCC8* mutations prevent the SUR1 protein from reaching the cell membrane, interfering with the proper formation of the K-ATP channel. Other mutations interfere with the K-ATP channel's function or its responses to outside molecules. Defective K-ATP channels lead to the constant release of insulin from beta cells. As a result, glucose is rapidly removed from the bloodstream. Without treatment, the hypoglycemia caused by congenital hyperinsulinism may result in serious complications such as intellectual disability and seizures.

#### permanent neonatal diabetes mellitus

At least 14 mutations in the *ABCC8* gene have been identified in people with permanent neonatal diabetes mellitus. Individuals with this condition often have a low birth weight and develop increased blood sugar (hyperglycemia) within the first 6 months of life.

*ABCC8* gene mutations that cause permanent neonatal diabetes mellitus change single amino acids in the protein sequence. These mutations result in K-ATP

channels that do not close, leading to reduced insulin secretion from beta cells and impaired blood sugar control.

#### other disorders

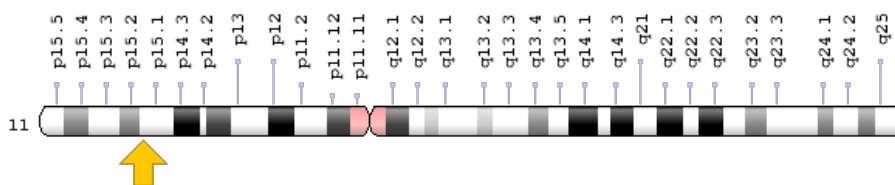
Other *ABCC8* gene mutations that have a relatively mild effect on K-ATP channel function as compared to that seen in permanent neonatal diabetes mellitus (see above) cause a condition called transient neonatal diabetes mellitus. Infants with this condition have hyperglycemia during the first 6 months of life, but their blood sugar returns to normal by age 18 months. However, affected individuals usually develop hyperglycemia again during adolescence or early adulthood. As in permanent neonatal diabetes mellitus, *ABCC8* gene mutations that cause transient neonatal diabetes mellitus interfere with K-ATP channel closure and lead to a reduction in insulin secretion.

Some studies suggest that normal variations (polymorphisms) in the *ABCC8* gene are associated with an increased risk of type 2 diabetes mellitus, the most common form of diabetes. Other studies, however, have not found an association between *ABCC8* gene variants and type 2 diabetes mellitus. People with this disease have hyperglycemia because the body does not respond correctly to the insulin secreted from beta cells. Although changes in the *ABCC8* gene may be associated with type 2 diabetes mellitus, a combination of lifestyle, genetic, and environmental factors all play a part in determining the risk of this complex disorder.

### **Chromosomal Location**

Cytogenetic Location: 11p15.1, which is the short (p) arm of chromosome 11 at position 15.1

Molecular Location: base pairs 17,392,885 to 17,476,870 on chromosome 11 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

### **Other Names for This Gene**

- ABC36
- ABCC8\_HUMAN

- ATP-binding cassette, sub-family C (CFTR/MRP), member 8
- ATP-binding cassette, sub-family C, member 8
- MRP8
- SUR
- SUR1
- TNDM2

## **Additional Information & Resources**

### Educational Resources

- Madame Curie Bioscience Database (Landes Bioscience, 2000-2011): Insulin Exocytosis in Pancreatic Beta Cells  
<https://www.ncbi.nlm.nih.gov/books/NBK6433/#A59214>
- The Human ATP-Binding Cassette (ABC) Transporter Superfamily: ABCC Genes  
<https://www.ncbi.nlm.nih.gov/books/NBK3/#A191>

### GeneReviews

- Familial Hyperinsulinism  
<https://www.ncbi.nlm.nih.gov/books/NBK1375>
- Permanent Neonatal Diabetes Mellitus  
<https://www.ncbi.nlm.nih.gov/books/NBK1447>

### Genetic Testing Registry

- GTR: Genetic tests for ABCC8  
<https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6833%5Bgeneid%5D>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28ABCC8%5BTI%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>

### OMIM

- ATP-BINDING CASSETTE, SUBFAMILY C, MEMBER 8  
<http://omim.org/entry/600509>
- DIABETES MELLITUS, TRANSIENT NEONATAL, 2  
<http://omim.org/entry/610374>

## Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
[http://atlasgeneticsoncology.org/Genes/GC\\_ABCC8.html](http://atlasgeneticsoncology.org/Genes/GC_ABCC8.html)
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=ABCC8%5Bgene%5D>
- HGNC Gene Family: ATP binding cassette subfamily C  
<http://www.genenames.org/cgi-bin/genefamilies/set/807>
- HGNC Gene Symbol Report  
[http://www.genenames.org/cgi-bin/gene\\_symbol\\_report?q=data/hgnc\\_data.php&hgnc\\_id=59](http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=59)
- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/6833>
- UniProt  
<http://www.uniprot.org/uniprot/Q09428>

## **Sources for This Summary**

- OMIM: ATP-BINDING CASSETTE, SUBFAMILY C, MEMBER 8  
<http://omim.org/entry/600509>
- Bennett K, James C, Hussain K. Pancreatic  $\beta$ -cell KATP channels: Hypoglycaemia and hyperglycaemia. *Rev Endocr Metab Disord*. 2010 Sep;11(3):157-63. doi: 10.1007/s11154-010-9144-2. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/20878482>
- Edghill EL, Flanagan SE, Ellard S. Permanent neonatal diabetes due to activating mutations in ABCC8 and KCNJ11. *Rev Endocr Metab Disord*. 2010 Sep;11(3):193-8. doi: 10.1007/s11154-010-9149-x. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/20922570>
- Ellard S, Flanagan SE, Girard CA, Patch AM, Harries LW, Parrish A, Edghill EL, Mackay DJ, Proks P, Shimomura K, Haberland H, Carson DJ, Shield JP, Hattersley AT, Ashcroft FM. Permanent neonatal diabetes caused by dominant, recessive, or compound heterozygous SUR1 mutations with opposite functional effects. *Am J Hum Genet*. 2007 Aug;81(2):375-82. Epub 2007 Jun 29.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17668386>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1950816/>
- Flanagan SE, Clauin S, Bellanné-Chantelot C, de Lonlay P, Harries LW, Gloyn AL, Ellard S. Update of mutations in the genes encoding the pancreatic beta-cell K(ATP) channel subunits Kir6.2 (KCNJ11) and sulfonylurea receptor 1 (ABCC8) in diabetes mellitus and hyperinsulinism. *Hum Mutat*. 2009 Feb;30(2):170-80. doi: 10.1002/humu.20838. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/18767144>
- Flanagan SE, Patch AM, Mackay DJ, Edghill EL, Gloyn AL, Robinson D, Shield JP, Temple K, Ellard S, Hattersley AT. Mutations in ATP-sensitive K<sup>+</sup> channel genes cause transient neonatal diabetes and permanent diabetes in childhood or adulthood. *Diabetes*. 2007 Jul;56(7):1930-7. Epub 2007 Apr 19. Erratum in: *Diabetes*. 2008 Feb;57(2):523.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17446535>

- Gloyn AL, Siddiqui J, Ellard S. Mutations in the genes encoding the pancreatic beta-cell KATP channel subunits Kir6.2 (KCNJ11) and SUR1 (ABCC8) in diabetes mellitus and hyperinsulinism. *Hum Mutat.* 2006 Mar;27(3):220-31. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16416420>
- Huopio H, Shyng SL, Otonkoski T, Nichols CG. K(ATP) channels and insulin secretion disorders. *Am J Physiol Endocrinol Metab.* 2002 Aug;283(2):E207-16. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/12110524>
- Pinney SE, MacMullen C, Becker S, Lin YW, Hanna C, Thornton P, Ganguly A, Shyng SL, Stanley CA. Clinical characteristics and biochemical mechanisms of congenital hyperinsulinism associated with dominant KATP channel mutations. *J Clin Invest.* 2008 Aug;118(8):2877-86. doi: 10.1172/JCI35414.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/18596924>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2441858/>
- Sandal T, Laborie LB, Brusgaard K, Eide SA, Christesen HB, Søvik O, Njølstad PR, Molven A. The spectrum of ABCC8 mutations in Norwegian patients with congenital hyperinsulinism of infancy. *Clin Genet.* 2009 May;75(5):440-8.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/19475716>

---

Reprinted from Genetics Home Reference:  
<https://ghr.nlm.nih.gov/gene/ABCC8>

Reviewed: January 2014

Published: February 14, 2017

Lister Hill National Center for Biomedical Communications  
U.S. National Library of Medicine  
National Institutes of Health  
Department of Health & Human Services